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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,071	08/22/2003	Philip A. Swain	11662-003-999	9609

20583 7590 08/26/2008

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
08/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/647,071	SWAIN ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 12, 2008 and August 15, 20008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *125,126,128,131-138,141 and 142* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *125,126,128,131-138,141 and 142* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-99, 105-108, and 110 were canceled, claims 101-103 and 109 were amended, and new claims 111-124 were added in the amendment to the claims received on June 1, 2006.

The amendment to the claims received on February 16, 2007 amended claims 100-101, 118; canceled claims 102, 114-116; and added new claims 125-140.

The amendment to the claims received on October 9, 2007 canceled claims 100-101, 103-104, 109, 111-113, 117-124, 127, and 130 and amended claims 125 and 129.

The amendment to the claims received on June 12, 2008 amended claim 125, canceled claims 129 and 139-140, and added new claims 141-142.

Claims 125-126, 128, 131-138, and 141-142 are currently pending and under consideration.

Election/Restrictions

2. Applicants elected, with traverse, Group I (previous claims 100-104) in the reply filed on June 1, 2006. The traversal was on the ground(s) that a serious burden to search Groups I and III did not exist. The traversal was found persuasive. Therefore, the restriction between Groups I and III (i.e. previous claim 109) was withdrawn. However, applicants did not traverse the restriction between Group I and Groups II or IV. The restriction was made final in the Office action mailed on August 17, 2006.

Priority

3. The present application claims status as a CON of 10/115,580 filed April 1, 2002 which is a CON of 09/882,803 filed June 14, 2001 which is a CON of 09/257,821 filed February 25, 1999 which is a CON of 08/720,487 filed September 30, 1996 (now U.S. Patent 5,876,727) which is a CIP of 08/563,673 filed November 28, 1995 (now U.S. Patent 5,760,184) which is a CIP of 08/414,971 filed March 31, 1995.

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/414,971, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 08/414,971 does not disclose nicotine or nicotine derivatives (i.e. nicotine metabolites of present Figure 19, nicotine-1'-N-oxide, trans-3'-hydroxycotinine, or nicotine glucuronide). In addition, application No. 08/414,971 does not disclose branches CJ 1.3 or CJ 11.

The disclosure of the prior-filed application, Application No. 08/563,673, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 08/563,673 (U.S. Patent 5,760,184 does not disclose nicotine derivatives (i.e. nicotine metabolites of present Figure 19, nicotine-1'-N-oxide, trans-3'-hydroxycotinine, or nicotine glucuronide). In addition, application No. 08/563,673 does not disclose branches CJ 1.3 or CJ 11.

Therefore, the priority date for the present claim limitations of nicotine derivatives, CJ 1.3, and CJ 11 is September 30, 1996 (i.e. filing date of U.S. application 08/720,487 which is now U.S. Patent 5,876,727). The priority date for the claim limitation of nicotine is November 28, 1995 (i.e. filing date of U.S. application 08/563,673 which is now U.S. Patent 5,760,184). Therefore, the priority for the presently claimed invention as a whole is September 30, 1996.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on June 12, 2008 is being considered by the examiner.

Invention as Claimed

6. A hapten-carrier conjugate comprising at least one hapten which is nicotine or a nicotine derivative and a carrier which is a bacterial toxin and wherein the hapten and the carrier are linked by a branch selected from the group of chemical moieties CJ 0 – CJ 11 and variations thereof.

Please note: claims 137-138 are considered intended use claims (i.e. suitable for parenteral, oral, dermal, or topical administration). Please refer to MPEP § 2106 which reads: "Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. The following are examples of language that may raise a question as to the limiting effect of the language in a claim: (A) statements of intended use or field of use".

Withdrawn Objection

7. The objection of claims 125-126, 128-129, and 131-140 regarding Markush groups in an improper format is withdrawn in view of the claim amendments received on June 12, 2008.

Withdrawn Rejections

8. The rejection of claims 125-126, 128-129, and 131-140 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement regarding the new matter of nicotine salts and nicotine derivative salts is withdrawn in view of the claim amendments received on June 12, 2008.

9. The rejection of claims 125-126, 128-129, 131-132, and 136-140 under 35 U.S.C. 103(a) as being unpatentable over Walling et al. U.S. Patent 5,164,504 issued November 17, 1992 and Glenn et al. U.S. Patent 5,980,898 with an effective filing date of November 14, 1996 is withdrawn due to an inadvertent error.

10. The rejection of claims 133-135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walling et al. U.S. Patent 5,164,504 issued November 17, 1992 and Glenn et al. U.S. Patent 5,980,898 with an effective filing date of November 14, 1996 as applied to claims 125-126, 128-129, 131-132, and 136-140 above, and further in view of Layton et al., Factors influencing the immunogenicity of the haptenic drug chlorhexidine in mice, Immunology 59: 459-465, 1986 is withdrawn due to an inadvertent error.

11. The rejection of claims 125-126, 128, and 131-140 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-5, 8-12, and 17-18 of U.S. Patent No. 5,876,727 is withdrawn in view of the terminal disclaimer received on August 15, 2008.

12. The rejection of claims 125-126, 129, and 131-140 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 88-127 of copending Application No. 11/472,215 is withdrawn in view of the terminal disclaimer received on August 15, 2008.

13. The rejection of claims 125, 128-129, and 131-140 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 88-118 of copending Application No. 11/472,220 is withdrawn in view of the claim amendments received for U.S. application 11/472,220.

Maintained Rejections

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Please note: the rejections may have been altered to reflect the claim amendments received on June 12, 2008.

Claim Rejections - 35 USC § 112

15. Claims 125-126, 128, 131-138, and 141-142 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention.

Independent claim 125 recites the following limitations: at line 3, "a carrier which is a bacterial toxin" and at the last three lines, "Q is a bacterial toxin or another branch identified by its "CJ" reference number". Thus, it is not clear from the claim limitations if the initial bacterial toxin carrier recited in the claims is Q (e.g. structure of nicotine-CJ-carrier, Q is redundant in CJ, etc.) or if Q is a second carrier (e.g. structure of nicotine-CJ/carrier-carrier, two carriers required by CJ0 - CJ 1.2, CJ 2 - CJ 2.1, CJ 3 - CJ 8.1, and CJ 10 - CJ 11). Further exacerbating the indefinite nature of the claim is the recitation at lines 5-6 that "said hapten and said carrier" (i.e. bacterial toxin carrier) "are linked by a branch selected from the group of chemical moieties identified by CJ reference number consisting of:" CJ 0 to CJ 11 wherein CJ 0 - CJ 1.2, CJ 2 - CJ 2.1, CJ 3 - CJ 8.1, and CJ 10 - CJ 11 recite Q in the formula. In addition, claim 142 reads "the hapten carrier" and "a pharmaceutically acceptable carrier". Therefore, are two carriers required by the claim or is the "pharmaceutically acceptable carrier" the bacterial toxin carrier.

Arguments and Response

16. Applicants' arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claims 125-126, 128, 131-138, and 141-142 were considered but are not persuasive for the following reasons.

Applicants contend that the claim amendments received on June 12, 2008 render the rejection moot.

Applicants' arguments are not convincing since while the claim amendments received on June 12, 2008 clarified the claims in certain respects (e.g. all carriers are bacterial toxins, etc.), the precise structure claimed is still indefinite (e.g. one carrier, two carriers, etc.).

New Rejections

Claim Rejections - 35 USC § 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claim 142 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 142 recites the limitation "the hapten carrier" in line 1. There is insufficient antecedent basis for this limitation in the claim. "[T]he hapten-carrier conjugate" is suggested.

Claim Rejections – 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 125-126, 128, 131-138, and 141-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walling et al. U.S. Patent 5,164,504 issued November 17, 1992 and Vyas U.S. Patent 4,483,793 issued November 20, 1984.

For present claims 125-126 and 137-138, Walling et al. teach nicotine, cotinine, and cotinine derivative (i.e. nicotine derivative/metabolite) hapten-carrier conjugates wherein the hapten is cotinine, trans-3'-cotinine, or cotinine-N-oxide, the carrier can be various proteins or peptides, and the carrier is covalently bound to the hapten via direct linkage (i.e. CJ 0), $(CH_2)_2CONH$ (i.e. CJ 6 where n = 2), or as represented in Formula I (please refer to column 2) wherein X is a straight or branched chain, saturated or unsaturated, divalent radical which has from 1-10 carbon atoms and 1-2 hetero atoms selected from the group consisting of S, O, and NZ wherein Z is a C_1-C_3 alkyl group and Q is a functional group selected from –COOH, $-NH_2$, $-C(O)NHNH_2$, -O(CO)Cl, -CHO, -NCS, or –NCO (please refer to the entire specification particularly the abstract; Formulas I, IV, V, VI, , VII, VIII, IX, X, XI, XII, XV, and XVI; columns 1-8; Examples 1-8; claims 1-6; and Table 1). In addition, Walling et al. teach utilizing S, O, and NH molecules in the branches joining the hapten and the carrier (please refer to columns 2-6). Furthermore, Walling et al. teach utilizing the hapten-carrier conjugates as immugens and eliciting immune responses in various animals (please refer to column 6).

Regarding the limitations of claim 126 (i.e. n is from 3 to 20), MPEP § 2144.09 states the following: "homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by $-CH_2-$ groups) are generally of sufficiently close structural similarity

that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). See also *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978). Thus, the $(CH_2)_2CONH$ branch taught by Walling et al. (i.e. CJ 6 where n = 2; please refer to Examples 6-7; Formulas XV and XVI; and columns 2-6) is considered an obvious variant of CJ 6 where n = 3-20 (i.e. present claim 126).

The intended use of present claims 137-138 (i.e. suitable for parenternal, oral, dermal, or topical administration) does not alter the structure of the presently claimed hapten-carrier conjugate (please refer to MPEP § 2106). In addition, the Office does not have the facilities and resources to provide the factual evidence needed in order to determine if the nicotine derivative hapten-carrier conjugates taught by Walling et al. differ from a nicotine derivative hapten-carrier conjugate that is suitable for parenternal, oral, dermal, or topical administration as presently claimed (i.e. present claims 137-138). In the absence of evidence to the contrary, the burden is upon the applicant to prove that the nicotine derivative hapten-carrier conjugates as claimed are different from the ones taught by the prior art and to establish the patentable differences. See *in re Best* 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922(PTO Bd.Pat. App. & Int. 1989).

For present claims 131 and 136, Walling et al. teach various excipients and "auxiliary agents" (i.e. pharmaceutically acceptable excipient; please refer to Examples 1-3 and 6-8).

For present claim 132, Walling et al. teach pristine (i.e. adjuvant; please refer to column 7, lines 24-31).

However, Walling et al. does not teach bacterial toxin carriers or more than one hapten coupled to the carrier.

For present claims 125, 128, 131-138, and 141-142, Vyas teaches hapten-carrier conjugates wherein the hapten can be a dimer or on average 1 hapten per 500 MW, the carrier is preferably a bacterial toxin including tetanus toxoid or diphtheria toxoid, the hapten-carrier conjugate can be used as a vaccine and administered via injection or oral route, adjuvants including aluminum hydroxide and aluminum phosphate can be utilized, and use of physiologically acceptable bases or dispersions, saline, emulsions etc. (please refer to the entire specification particularly columns 1-7).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the nicotine derivative hapten-carrier conjugates taught by Walling et al. with the bacterial toxin carrier and multiple haptens taught by Vyas.

One having ordinary skill in the art would have been motivated to do this because Vyas teaches that bacterial toxin carriers and multiple haptens elicit a strong immune response (i.e. stronger than other carriers including KLH; please refer to paragraph spanning columns 6-7 and results table).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the nicotine derivative hapten-carrier conjugates taught by Walling et al. with the specific bacterial toxin carrier and multiple haptens taught by Vyas because of the results obtained by Vyas (please refer to paragraph spanning columns 6-7 and results table).

Therefore, the modification of the nicotine derivative hapten-carrier conjugates taught by Walling et al. with the specific bacterial toxin carrier and multiple haptens taught by Vyas render the instant claims *prima facie* obvious.

Conclusion

21. Regarding the arguments against Walling et al. (U.S. Patent 5,164,504), applicants appear to assert that a nicotine metabolite in not a nicotine derivative, this is not found persuasive because the present specification has not defined nicotine derivatives as excluding nicotine metabolites. In addition, regarding the "unexpected" results of the Phase II clinical trials, it is noted that (1) claims 125-126, 128, and 141 are drawn to a hapten-carrier conjugate only and not to a pharmaceutical, (2) the breadth of the claims is greater than the two specific formulations of NicVAX and TA-NIC, and (3) it is well known in the art that carriers and adjuvants can augment the immune system particularly in combination with haptens which by definition elicit a weak immune response. However, if applicants are aware if one carrier or formulation is advantageous (i.e. unexpectedly high antibody titer, only formulation that produces high antibody titer in humans, etc.) to other carriers or formulations, applicants are requested to submit evidence to support the advantage.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

August 19, 2008